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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Ballevre et al.
Appl. No.: 09/774,814
Conf. No.: 2493
Filed: January 30, 2001
Title: METHOD FOR MAINTAINING OR IMPROVING THE SYNTHESIS OF MUCINS
Art Unit: 1653
Examiner: S. Liu
Docket No.: 112701-136

Commissioner for Patents
Washington, DC 20231

RESPONSE TO OFFICE ACTION

Sir:

In response to the Office Action dated December 17, 2002, please amend the above-identified patent application as follows:

Please substitute the paragraph beginning on page 5 at line 12 with the following rewritten paragraph:

The invention is based on the finding that enterally administering nutritional composition which contains a protein source enriched in threonine has a beneficial effect on the synthesis of mucins. The protein source may be any suitable source of amino acids that is enriched in threonine. For example, the protein source may be milk protein, egg white, caseino-glyco-macropeptide, whey protein, casein protein, soy protein, rice protein, pea protein or oat protein, or mixtures of these proteins. Also, the protein source may be in the form of intact protein, hydrolyzed protein, or mixtures thereof. Further, if desired, the protein source may be in the form of free amino acids. In an embodiment, the protein may be in the form of mixtures of intact protein or hydrolyzed protein, with free amino acids.

A1

Please substitute the paragraph beginning on page 12 at line 27 with the following rewritten paragraph:

After 24 hours of metabolic labeling, the culture medium of cells was removed. Cells were washed twice with 10 ml of 1 X phosphate buffer solution (PBS) and recovered using a rubber scraper. Cells were homogenized in 0.05M Tris/HCl buffer pH 7.50 using a polytron at a low setting (6.000 rpm, 30 sec, 4°C). An aliquot of each homogenate was removed for the measurement of the specific radioactivity of the intracellular free threonine considered as the precursor pool. Mucoproteins were purified from the cell homogenates by a size exclusion chromatography after a partial enzymatic digestion of non-highly glycosylated and thus protected proteins. Purified mucins were hydrolyzed with 6M HCl (24h at 100°C), and their amino acid composition was determined by HPLC. The outlet of the UV detector was connected to a radioactive detector (Radiomatic 500TR, Packard) to measure the ^{3}H-threonine incorporated in mucoproteins. The fractional synthesis rate (FSR) of mucoproteins was calculated and expressed in percent/day (%/d): (FSR = (Specific radioactivity of mucoprotein bound threonine/Specific radioactivity of intracellular free threonine) * 100).

A2

Please substitute the paragraph beginning on page 14 at line 19 with the following rewritten paragraph:

Rat mucosal samples were gently homogenized in 0.05M Tris/HCl buffer pH 7.50 using a polytron at a low setting (6,000 rpm, 30 sec, 4°C). An aliquot of each sample homogenate was used to measure the 1-^{13}C-Valine enrichment in the intracellular pool that was considered as ^{13}C-enrichment of the precursor pool. Thereafter, mucoproteins were purified as described previously for the *in vitro* experiment. 1-^{13}C-Valine enrichments in mucoproteins were measured by mass spectrometry.

A3

In the Claims:

Please amend Claims 24, 28-31, 37 and 42 as follows:

24. (Amended) A method for maintaining the synthesis of mucins in a patient, the method comprising enterally administering to the patient a nutritional composition which has a protein source including amino acids wherein threonine comprises at least 7.4% by weight of the amino acids.

A4